

Kindly replace the paragraph beginning at Page 8, line 7 with the following:

B2

--The process may also be used for detecting the presence of an integrin subunit $\alpha 10$ comprising the amino acid sequence shown in SEQ ID No. 2 or SEQ ID No. 4, or of an integrin heterodimer comprising said subunit $\alpha 10$ and a subunit β , or of homologues or fragments thereof having similar biological activity.--

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Kindly replace the paragraph beginning on Page 8, line ~~23~~ with the following:

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In a still further embodiment this process is a process for detecting the presence of an integrin subunit $\alpha 10$, or of a homologue or fragment of said integrin subunit having similar biological activity, on cells, whereby a polynucleotide or oligonucleotide chosen from the group comprising a polynucleotide or oligonucleotide chosen from the nucleotide sequence shown in SEQ ID No. 1 is used as a marker under hybridisation conditions wherein said polynucleotide or oligonucleotide fails to hybridise to a DNA or RNA encoding an integrin subunit $\alpha 1$. Said cells may be chosen from the group comprising chondrocytes, smooth muscle cells, endothelial cells, osteoblasts and fibroblasts. Said integrin fragment may be a peptide chosen from the group comprising peptides of the cytoplasmic domain, the I-domain and the spliced domain, such as a peptide comprising the amino acid sequence (SEQ ID No.:7) , or a fragment comprising the amino acid sequence from about amino acid no. 952-to about amino acid no. 986 of SEQ ID No. 2, or a fragment comprising the amino acid sequence from about amino acid No. 140 to about amino acid no. 337 of SEQ ID No. 2.

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Kindly replace the paragraph beginning on Page 9, line ~~27~~ with the following:

B712

--The invention also relates to a process for determining the differentiation-state of cells during development, in pathological conditions, in tissue regeneration and in therapeutic and physiological reparation of cartilage, whereby a polynucleotide or oligonucleotide chosen from the nucleotide sequence shown in SEQ ID No. 1 is used as a marker under hybridisation conditions wherein said polynucleotide or oligonucleotide fails to hybridise to a DNA or RNA encoding an integrin subunit $\alpha 1$. Embodiments of this aspect

comprise a process, whereby said polynucleotide or oligonucleotide is a polynucleotide or oligonucleotide coding for a peptide chosen from the group comprising peptides of the cytoplasmic domain, the I-domain and the spliced domain, such as a polynucleotide or oligonucleotide coding for a peptide comprising the amino acid sequence (SEQ ID No.: 7), or comprising the amino acid sequence from about amino acid No. 952 to about amino acid no. 986 of SEQ ID No. 1, or the amino acid sequence from about amino acid No. 140 to about amino acid No. 337 of SEQ ID No. 1. Said pathological conditions may be any pathological conditions involving the integrin subunit $\alpha 10$, such as rheumatoid arthritis, osteoarthritis or cancer, or atherosclerosis or inflammation. Said cells may be chosen from the group comprising chondrocytes, smooth muscle cells, endothelial cells, osteoblasts and fibroblasts.--

Kindly replace the paragraph beginning on Page 14, line 34 and ending on Page 15, line 22 with the following:

B4 --The deduced amino acid sequence of $\alpha 10$ was found to share the general structure of the integrin α subunits described in previously published reports (6-21). The large extracellular N-terminal part of $\alpha 10$ contains a seven-fold repeated sequence which was recently predicted to fold into a β -propeller domain (32). The integrin subunit $\alpha 10$ contains three putative divalent cation-binding sites (DxD/NxD/NxxxD) (53), a single spanning transmembrane domain and a short cytoplasmic domain. In contrast to most α -integrin subunits the cytoplasmic domain of $\alpha 10$ does not contain the conserved sequence KXGFF (R/K) R. The predicted amino acid sequence in $\alpha 10$ is KLGFFAH. Several reports indicate that the integrin cytoplasmic domains are crucial in signal transduction (54) and that membrane-proximal regions of both α - and β -integrin cytoplasmic domains are involved in modulating conformation and affinity state of integrins (55-57). It is suggested that the GFFKR motif in α -chains are important for association of integrin subunits and for transport of the integrin to the plasma membrane (58). The KXGFFKR domain has been shown to interact with the intracellular protein calreticulin (59) and interestingly, calreticulin-null embryonic stem cells are deficient in integrin-mediated cell adhesion (60).

B4 It is therefor possible that the sequence (SEQ ID No.:9) in $\alpha 10$ have a key function in regulating the affinity between $\alpha 10\beta 1$ and matrix proteins.--

Kindly replace the paragraph beginning on Page 18, line 33 and ending on Page 19, line 13 with the following:

B5 --The degenerate primers (SEQ ID No.: 9) ((SEQ ID No.: 10), forward) and (SEQ ID No.: 11) ((SEQ ID No.: 12) reverse) were used in PCR (Camper et al, JBC, 273, 20383-20389 (1998) to amplify the nucleotide sequence corresponding to the bovine peptide 1 (Figure 2) . A 900 bp PCR-fragment was then amplified from bovine, cDNA using an internal specific primer (SEQ ID No.: 13) (SEQ ID No.: 14), forward) corresponding to the cloned nucleotide sequence of peptide 1 together with the degenerate primer (SEQ ID No.:15) ((SEQ ID No.:16) PGHWDR, reverse) corresponding to the bovine peptide 2 (Figure2). Mixed bases were used in positions that were twofold degenerate and inosines were used in positions that are three- or fourfold degenerate. mRNA isolation and CDNA synthesis was done as earlier described (Camper et al, JBC, 273, 20383-20389 (1998)). The purified fragment was cloned, purified and sequenced as earlier described (Camper et al, JBC, 273, 20383-20389 (1998)).--

Kindly replace the paragraph beginning on Page 19, line 28 and ending on Page 20, line 8 with the following:

B6 --The cloned 900bp PCR-fragment, corresponding to bovine $\alpha 10$ -integrin, was digoxigenin-labelled according to the DIG DNA label-ling kit (Boehringer Mannheim) and used as a probe for screening of a human articular chondrocyte λ ZapII cDNA library (provided by Michael Bayliss, The Royal Veterinary Basic Sciences, London, UK) (52) . Positive clones containing the pbluescript SK+ plasmid with the cDNA insert were rescued from the ZAP vector by *in vivo* excision as described in the ZAP-cDNA® synthesis kit (Stratagene). Selected plasmids were purified and sequenced as described earlier (Camper et al, JBC, 273, 20383-20389 (1998)) using T3, T7 and internal specific primers. To obtain CDNA that encoded the 5' end of $\alpha 10$ we designed the primer (SEQ ID No.:17)

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(reverse; residue 1254-1280 in α 10 CDNA) and used it. for rapid amplification of the CDNA 5' end (RACE) as described in the Marathon™ cDNA Amplification kit (Clontech INC., Palo Alto, CA).--

Kindly replace the paragraph beginning on Page 29, line 27 and ending on Page 30, line 9 with the following:

B7

--A plasmid for intracellular expression in E. coli of the alternatively spliced region (amino acid pos. 952-986, SEQ. ID 1) was constructed as described. The alternatively spliced region were back-translated using the E. coli high frequency codon table, creating a cDNA sequence of 96 % identity with the original sequence (SEQ. ID 1 nucleotide pos 2940-3044). Using sequence overlap extension (Horton et al., Biotechniques 8:528, 1990) primer α 10pfor (tab. I) and α 10pfor (tab. I) was used to generate a double stranded fragment encoding the α 10 amino acid sequence. This fragment was used as a PCR template with primers α 10pfor2 (tab. I) and α 10prev2 (tab. I) in order to generate restriction enzyme site for sub-cloning in a pET vector containing the Z-domain of staphylococcal protein A, creating a fusion of the α 10 spliced region with the amino terminal of the Z-domain with trombin cleavage site residing in-between. The fragment generated in the second PCR reaction is shown (SEQ ID No. 5) also indicating the unique restriction enzymes used for sub-cloning in the expression vector.--
